**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| In re Application of: | ) | Confirmation No.: 9264 |
| | ) | |
| Yitzchak HILLMAN | ) | Art Unit: 1633 |
| | ) | |
| I.A. Filing Date: 12/21/2003 | ) | Examiner: J. L. EPPS FORD |
| 371(c) Date: June 17, 2005 | ) | |
| | ) | October 9, 2007[1] |
| U.S. Appln. No.: 10/539,558 | ) | |
| | ) | ATTY.'S DOCKET: HILLMAN=1 |
| For: DISEASE TREATMENT VIA ANTIMICROBIAL PEPTIDE… | ) | |

**REPLY TO RESTRICTION AND ELECTION REQUIREMENTS**

Customer Service Window, Mail Stop **Amendment**
Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Randolph Building
401 Dulany Street
Alexandria, Virginia 22314

Sir:

The applicant is in receipt of the Office Action mailed August 8, 2007, to which applicant replies below. A petition for one month's extension of time and the one month's late fee are attached hereto.

Acknowledgement by the PTO of the receipt of applicant's papers filed under §119 **would be appreciated**.

Restriction has been required among what the PTO deems as being ten (10) separate inventions according to PCT Rules 13.1 and 13.2, as follows:

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[1] Monday, October 8, 2007, was a Federal holiday, Columbus Day, so this Reply is timely filed on Tuesday, October 9, 2007.

**Group (a):** Claims 100-112, drawn to an article of manufacture and a method of treating a disease in a subject in need thereof, the method comprising providing to the subject a therapeutically effective amount of a compound being capable of decreasing an activity and/or level of an antimicrobial peptide (AMP) and/or AMP-like molecule, thereby treating the disease in the subject in need thereof, wherein said compound is a molecule capable of binding said AMP and/or AMP-like molecule, and wherein the molecule is an antibody or an antibody fragment.

**Groups (b)-(i):** Claims 100-101, 103-107 and 109-112, drawn to an article of manufacture and a method of treating a disease in a subject in need thereof, the method comprising providing to the subject a therapeutically effective amount of a compound being capable of decreasing an activity and/or level of an AMP and/or AMP-like molecule, thereby treating the disease in the subject in need thereof, wherein the compound is:

(b) an enzyme capable of cleaving said AMP and/or AMP-like molecule;

(c) an siRNA molecule capable of inducing degradation of an mRNA encoding said AMP and/or AMP-like molecule;

(d) a DNAzyme capable of cleaving an mRNA or DNA encoding said AMP and/or AMP-like molecule;

(e) an antisense polynucleotide capable of hybridizing with an mRNA encoding said AMP and/or AMP-like molecule;

(f) a ribozyme capable of cleaving an mRNA encoding said AMP and/or AMP-like molecule;

(g) a non-functional analogue of at least a functional portion of said AMP and/or AMP-like molecule;

(h) a molecule capable of inhibiting activation or ligand binding of said AMP and/or AMP-like molecule; and

(i) a triplex-forming oligonucleotide capable of hybridizing with a DNA encoding said AMP and/or AMP-like molecule.

**Group (j):** Claims 113-121, drawn to an article of manufacture and a method of treating a disease in a subject in need thereof, the method comprising providing to the subject a therapeutically effective amount of an AMP and/or AMP-like molecule, thereby treating the disease in the subject in need thereof.

As applicant must make an election, even if the requirement is traversed, applicant hereby respectfully and

provisionally elects Group (j), presently comprising claims 113 to 121, with at least partial traverse and without prejudice.

First, applicant does not dispute that Group (j) defines an invention which is patnetably distinct from the claims of the other groups, but applicant does not acquiesce in the holding that each of the non-elected groups (a) through (i) define separate inventions from one another.

Applicant respectfully submits that the requirement should be reconsidered on the following basis. Although some of the inventions of Groups (a)-(j) are drawn to methods wherein a compound capable of decreasing an activity and/or level of an AMP and/or AMP-like (AML) molecule is used; and the other inventions are drawn to methods wherein an AMP and/or AML is used, all these inventions relate to regulation of activity and/or level of an AMP or an AML, to thereby regulate a process such as growth, differentiation, inflammation, metastasis and/or angiogenesis in a cell/tissue, and this is, in fact, the common technical feature of all these inventions.

As particularly defined by the present application, the "regulator" relates either to an AMP/AML or to a compound capable of decreasing an activity and/or level of an AMP/AML

(page 23, lines 17-19); and the method may be effected using a single regulator or any combination of multiple regulators (page 24, lines 3-4).

Furthermore, in certain cases, the compound capable of decreasing activity and/or level of an AMP as defined by the present application is, in fact, an AMP itself. In such a particular case, administration of the anti-inflammatory cathelicidin pro-peptide may be used in order to inhibit the pro-inflammatory fragments thereof by competing with said fragments on receptor activation, as also described in page 24, lines 17-19 of the description.

Reconsideration of the requirement and at least partial withdrawal thereof is therefore believed to be in order and is respectfully requested.

In addition to the aforementioned restriction requirement, the PTO has also required an election of species. Again, as applicant must make an election even if the requirement is traversed, applicant hereby respectfully and provisionally elects as the AMP and/or AMP-like molecule "LL-37" with traverse and without prejudice[2]; and as the general type of disease, "inflammatory disease", again with traverse and without prejudice.

[2] FALL-39 is a cathelicidin closely related to LL-37, and should be considered with it.

The claims which read on the elected active agent within the elected Group (j) are claims 113, 114, 116, 117, 118, 120 and 121; and the claims which read on inflammatory disease are claims 113-116 and 118-120.

(1) Claims 110, 116 and 120 recite several species of AMP, namely, beta-defensin-1, beta-defensin-2 and LL-37; however, these AMPs are only the preferred examples of broader categories of AMPs, namely defensins and cathelicidines, as defined in the present application (see, e.g., page 38, line 33-page 39, line 3; and the paragraph bridging pages 63-64 with specific respect to LL-37 as an example of cathelicidin).

(2) FALL-39 is a human cathelicidin peptide, mentioned in the description (page 66, lines 7-8), which contains two amino acids (FA) joined to LL-37, and is thus a pro-peptide of LL-37 and a part of the longer cathelicidin hCAP-18. FALL-39 was described, e.g., in Agerberth *et al.*, *PNAS USA*, 1995, 92, 195-199 (see in particular Fig. 1 on page 196), mentioned in the description (en electronic copy is enclosed).

(3) Because of the close relationship between LL-37, the two should be considered together, and applicant so requests.

(4) Claims 105, 111, 117 and 121 recite several species of disease; however, none of these claims specifically calls for an inflammatory disease. Nevertheless, as stated in the present application, the claimed method can be used for treating any of various diseases, in particular, diseases which are associated with (i) a tumor; (ii) inflammation; (iii) an epithelial wound; (iv) dysregulation of growth/differentiation of a cell/tissue; (v) dysregulation of growth/differentiation balance of a cell/tissue; and (vi) diseases associated with angiogenesis (see, e.g., page 45, lines 3-8 and page 67, lines 25-29). As further defined by the present application, arthritis in general, and rheumatoid arthritis in particular, are inflammatory diseases (see, e.g., page 75, lines 31-32). Applicant reserves the right to specifically claim inflammatory diseases.

As the requirements place a very great burden on the applicant, and as the various aspects of the invention(s) are

claimed so closely related, applicant respectfully requests favorable reconsideration.

Respectfully submitted,

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